(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 November 2001 (08.11.2001)

PCT

(10) International Publication Number
WO 01/84120 A2

(51) International Patent Classification[7]: G01N 21/00

(21) International Application Number: PCT/US01/14292

(22) International Filing Date: 2 May 2001 (02.05.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/564,140 3 May 2000 (03.05.2000) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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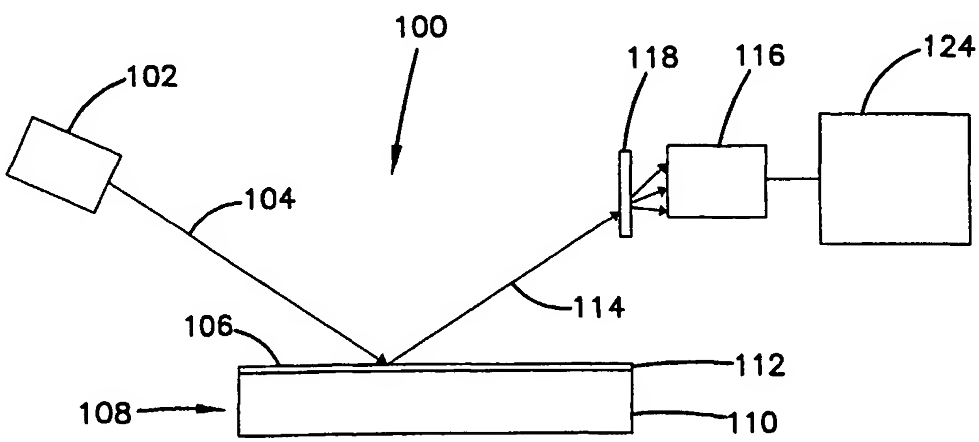
Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND DEVICES FOR SIGNAL POSITION ANALYSIS



(57) Abstract: A method of detecting a deviation from a baseline of a signal includes generating at least one pair of Fourier coefficients from the signal. A phase angle is then determined from a pair of the Fourier coefficients and the phase angle is correlated to the position of the deviation from the baseline of the signal. Another embodiment is an apparatus that includes a processor that is configured and arranged to carry out the steps in the method. The method and apparatus can be used to analyze a variety of signals including optical spectra and telecommunications signals. One particular exemplified example is the analysis of surface plasmon resonance signals.

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METHODS AND DEVICES FOR SIGNAL POSITION ANALYSIS

This application is being filed as a PCT International Patent application in the name of Quantech Ltd., a US national corporation, designating all countries except the US, on 02 May 2001.

Field of the Invention

This invention relates to methods and devices for determining a position of a deviation from a baseline in a signal. In addition, the invention relates to methods and devices for determining a position of a deviation from a baseline of a surface plasmon resonance spectrum.

Background of the Invention

A variety of signals obtained from detection devices include a baseline with single or multiple deviations (e.g., peaks or notches) from the baseline of the signal. In many instances, the position of the deviation within the signal provides useful information. Examples of such instances include optical spectra. The position of peaks or notches in an optical spectrum can be used, for example, to determine the presence or absence of particular functional groups or the amount or concentration of an analyte in a sample. In some instances, the position of the deviation is compared to a known or standard sample to determine if the position of the deviation has changed. These methods can be used, for example, to develop assays for particular components or analytes in a sample.

Surface plasmon resonance provides one example of a technique that utilizes the determination of a position of a deviation in a signal to indicate the amount or concentration of an analyte in a sample. In particular, as described, for example, in U.S. Patents Nos. 4,931,384; 4,828,387; 4,882,288; 4,992,385; 5,118,608; and 5,310,686, PCT Patent Applications Publication Nos. WO 88/07202 and WO 88/10418, and UK Patent Application Publication No. GB 2 202 045, all of which are incorporated herein by reference, the shift of a notch in a surface plasmon resonance spectrum can be correlated to the amount of an analyte in a sample.

Methods have been developed to determine the position of deviations from a baseline. Such methods include, for example, electrical circuitry or computer programming that determines when a signal crosses a threshold value. Alternatively, the absolute maximum or minimum measured value may be selected. Accuracy of these measurements may be improved using signal refinement techniques such as, for example, smoothing techniques. These methods may, however, not provide sufficiently accurate information because they do not

determine the deviation center point, do not detect deviations that are lower than the threshold limit, or are too sensitive to noise.

Summary of the Invention

Generally, the present invention relates to novel methods and devices for the determination of a position of a deviation from a baseline in a signal such as a surface plasmon resonance signal. One embodiment is a method of detecting of a deviation from a baseline of a signal. The method includes generating at least one pair of Fourier coefficients from the signal. A phase angle is then determined from a pair of the Fourier coefficients and the phase angle is correlated to the position of the deviation from the baseline of the signal. Another embodiment is an apparatus that includes a processor that is configured and arranged to carry out the steps in the method. The method and apparatus can be used to analyze a variety of signals including optical spectra and telecommunications signals. One particular exemplified example is the analysis of surface plasmon resonance signals.

Typically, although not necessarily, the method is accomplished by Fourier transforming the signal using any Fourier Transform technique, including, for example, Fast Fourier Transform techniques. As an example, the Fourier coefficients, $y_{p,r}$ and $y_{p,i}$, are given by the following formulas:

$$y_{p,r} = \sum_{k=0}^{N-1} x_k \cos(2\pi kp / N)$$

$$y_{p,i} = \sum_{k=0}^{N-1} x_k \sin(2\pi kp / N)$$

where the signal contains N discrete points, k = 0, 1, 2, ..., N-1, with associated signal magnitudes, x_k, and p is an integer selected from the group of integers ranging from 1 to N-1. In this instance, the phase angle, ϕ_p, for a desired value of p>0 (e.g., p=1) is given by the expression: $\phi_p = \arctan(y_{p,i}/y_{p,r})$. In at least some embodiments, an unrefined signal from a detection device is further refined (e.g., smoothed over a window, clipped, or convoluted with a background signal, or combinations thereof) prior to determination of the pair of Fourier coefficients from the refined signal.

The above summary of the present invention is not intended to describe each disclosed embodiment or every implementation of the present invention. The Figures and the detailed description which follow more particularly exemplify these embodiments.

Brief Description of the Drawings

The invention may be more completely understood in consideration of the following detailed description of various embodiments of the invention in connection with the accompanying drawings, in which:

Figure 1 is a schematic illustration of a surface plasmon resonance device;

Figure 2 is a schematic illustration of an expanded view of a test element of the surface plasmon resonance device of Figure 1;

Figure 3 is a top view of one embodiment of a test element with multiple testing regions, according to the invention;

Figure 4 is an example of a signal having a deviation from a baseline;

Figure 5 is a graph of 31 signals, each signal having a deviation spaced apart from the other signals;

Figure 6 is a graph of the position determined for the deviation of each of the 31 signals of Figure 5, as determined according to the invention;

Figure 7 is an example of a surface plasmon resonance signal;

Figure 8 is an example of a surface plasmon resonance background signal;

Figure 9 is a graph of a convolution of the signals of Figures 7 and 8, according to the invention;

Figure 10 is a graph of the signal of Figure 9 after an odd-even refinement is applied, according to the invention;

Figure 11 is a graph of the signal of Figure 10 after a smoothing refinement is applied, according to the invention;

Figure 12 is a graph of the signal of Figure 11 after a normalization refinement is applied, according to the invention; and

Figure 13 is a graph of the signal of Figure 12 after a clipping refinement is applied, according to the invention.

While the invention is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the invention to the particular embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention.

Detailed Description of the Preferred Embodiment

The present invention is believed to be applicable to methods and devices for determining a position of a deviation from a baseline in a signal. The present invention is also directed to methods and devices for determining a position of a deviation from a baseline of an optical spectrum, such as a surface plasmon

resonance spectrum. While the present invention is not so limited, an appreciation of various aspects of the invention will be gained through a discussion of the examples provided below.

The novel methods described below for determining a position of a deviation from a baseline in a signal are described in relation to their use in surface plasmon resonance assay techniques. This provides one example of the methods and their application which are, however, applicable to techniques other than surface plasmon resonance assays.

Surface Plasmon Resonance

Figure 1 is a schematic illustration of one embodiment of a surface plasmon resonance device 100. The device 100 includes a light source 102 that shines light 104 toward a surface 106 of a test element 108. The test element 108 includes a base 110 and a reflective metal layer 112 that defines the surface 106. Typically (except at or near the surface plasmon resonance frequency), the light 104 is substantially completely reflected (to form reflected light 114) toward a detection device 116. In the illustrated embodiment, light 104, 114 includes multiple wavelengths and the device includes a diffractive element 118 to separate the light by wavelength prior to reaching the detection device 116 so that a wavelength-dependent spectrum is obtained.

At or near the surface plasmon resonance frequency, the irradiating photons of light 104 interact with the conduction band electrons in the reflective metal layer 112 to generate surface plasmons. This substantially reduces or eliminates the intensity of reflected light 114 at that frequency. The conduction band electrons in the reflective metal layer act, at least in part, as a "plasma" with a fixed background of positive ions. The surface plasmon represents a quantum of oscillation of surface charges generated by the conduction band electrons that behave like a quasi-free electron gas.

Other methods and devices for surface plasmon resonance detection can be used, including, for example, methods and devices described in U.S. Patents Nos. 4,931,384; 4,828,387; 4,882,288; 4,992,385; 5,118,608; and 5,310,686, PCT Patent Applications Publication Nos. WO 88/07202 and WO 88/10418, and UK Patent Application Publication No. GB 2 202 045, all of which are incorporated herein by reference. As an example of an alternative detection scheme, some of the references cited above describe a device that observes transmitted light instead of reflected light. These alternative embodiments can be used to generate surface plasmon resonance signals for analysis as described below.

Figure 2 schematically illustrates an expanded view of the cross-section of the test element 108. For light to interact with conduction band electrons in the reflective metal layer 112 resulting in energy transfer from photons to surface plasmons, there must be a match between the energy and momentum of the photons and surface plasmons. For a flat metal surface, there is no wavelength of light that matches these conditions. However, if the metal surface is no longer flat, the momentum of the photons is altered. Although surface roughening can be used, two simple structures are often employed to alter photon momentum. These two structures are prisms and gratings. Figure 2 illustrates a surface 106 that is altered by the formation of a sinusoidal grating. It will be recognized, however, that other gratings, including, for example, square well and triangular well gratings, can also be used. As an example, a sinusoidal grating can be prepared with peak-to-peak distances (which are typically on the order of the wavelength of light illuminating the surface) ranging from, for example, 200 to 800 nm and peak-to-valley distances ranging from, for example, 20 to 100 nm. It will be recognized that surfaces with prisms, instead of gratings, are also suitable.

The base layer 110 is typically made from plastic or glass. Suitable plastics include, for example, polycarbonates and polymethylmethacrylate. Typically, the grating is formed in the surface of the base layer 110 by techniques, such as, for example, injection molding, etching, scoring, compression molding, and other known techniques. It may be advantageous to form the grating in the base layer because the base layer is a thicker bulk material, while the refractive metal layer is relatively thin. However, in some embodiments, the base layer is smooth and the grating is formed by modifying (e.g., etching or scoring) the reflective metal layer.

The reflective metal layer 112 is disposed on the base layer 110. The reflective metal layer can be formed by a variety of techniques including, for example, chemical or physical vapor deposition, sputtering, electroplating, or electroless plating. If the base layer defines a grating,, a technique is used that forms the reflective metal layer 112 as a conformal layer on the base layer 110. The thickness of the reflective metal layer 112 can range from, for example, 30 to 120 nm and is generally less than about 50 nm.

Although the reflective metal layer 112 can be formed using any material that has conduction band electrons, the preferred materials are highly reflecting, do not form oxide, sulfide or other films upon atmospheric exposure, and are compatible with the chemistries used to perform the assays. Suitable metals include, for example, gold, indium, copper, platinum, silver, and chrome. Gold is particularly suitable because it is resistant to oxidation and other atmospheric contaminants, but can still be reacted to bind with a test material.

The surface plasmon resonance frequency and the coupling of the photons to the conduction band electrons in the reflective metal layer depend on a variety of factors including the nature of the material of the reflective metal layer, the structure of the reflecting surface of the conductive material (including the peak-to-peak distance and peak-to-valley distance of the grating), and the presence of other materials on the reflecting surface. One assay includes depositing a test material 120 onto the surface 106 of the reflective metal layer 112. The test material 120 is typically bound to the surface by covalent, ionic, coordinative, or hydrogen bonding or combinations thereof. A variety of methods for bonding such test materials to a reflective metal surface are known.

In an assay, the test material 120 selectively binds to a desired analyte 122. Selective binding methods include forming covalent, ionic, coordinative, hydrogen or van der Waals bonds or combinations thereof between the test material and the analyte or adsorbing or absorbing the analyte on the test material. As non-limiting examples, the test material 120 can be an antigen, antibody, hormone, hormone receptor, polynucleotide strand, avidin or strepavidin, biotin, protein A, immunoglobulin, enzyme, enzyme cofactor or inhibitor, etc. to selectively bind to an associated analyte. The particular test material and analyte can be chosen to provide, for example, immunological, nucleic acid binding, enzymatic, chemical, or gas adsorption assays for use in fields such as, for example, agriculture, food testing, biological and chemical agent testing, and chemical and biological process monitoring.

The capturing of the analyte by the test material on the surface of the reflective metal layer typically alters the position (e.g., wavelength) of the surface plasmon resonance. Generally, the magnitude of the change in position of the surface plasmon resonance reflects the amount of analyte captured by the test material which in turn typically reflects the amount or concentration of the analyte in a test sample. In at least some instances, the relationship between the position of the surface plasmon resonance and the amount of analyte in the sample is linear. The determination of the concentration or amount of an analyte in a sample can be made from the determination of a shift from the surface plasmon resonance frequency without the analyte. Alternatively, one or more calibration (e.g., known) samples or a calibration curve can be used to assist in determining the concentration or amount of analyte based on the measured frequency itself or the shift in frequency.

Referring again to Figure 1, in the illustrated embodiment, the light source 102 is typically a multi-wavelength light source, such as, for example, a lamp. Typically, the light 104 from the light source 102 is collimated and polarized prior to arriving at the surface 106 of the test element 108. The light is collimated to limit

the range of angles at which the light intersects the surface 106 of the test element 108. The light is polarized because only p-polarized light interacts with the conduction band electrons. Light sources that produce visible, infrared, or ultraviolet light, or a combination thereof can be used. As an example, a light source can be used that has a wavelength range of 700 to 800 nm.

In some embodiments, multiple light sources or multiple beams from a single light source (formed using, for example, multiple apertures in a screening element) are directed toward the test element 108. These beams 104a, 104b, 104c can be directed to different regions 126a, 126b, 126c of the test element 108, as illustrated in Figure 3. For example, the beams can be directed to regions (e.g., regions 126a, 126b) of the test element with different samples. One beam may be directed to a region (e.g., region 126c) upon which the test material and the sample are deposited, but where there is no grating to couple the photons with the conduction band electrons.

In the illustrated embodiment, a diffraction element 118 is used to separate the reflected light into the component wavelengths. This light is then detected using a detection device 116, such as, for example, a CCD (charge-coupled device) array. A CCD array includes an array of individual detectors arranged in columns and rows. The embodiment illustrated in Figure 1 illustrates the wavelengths of light being distributed along at least one column of the CCD array (in another embodiment, the diffraction element distributes the light along at least one row of the CCD array). When multiple beams of light are used, each beam of light will illuminate different column(s) of the CCD array. The signal (associated with a single beam of light from the light source) along the appropriate column(s) of the CCD array represents a surface plasmon resonance frequency spectrum of intensity versus wavelength, as illustrated in Figure 7. This and any other spectrum (e.g., a background spectrum or spectra for other samples) are provided to a processor 124 that utilizes the methods described below to analyze the signal.

As an alternative, a single wavelength light source can be used. In this embodiment, the angle that the light intersects the surface of the test element is varied and a signal corresponding to reflected light intensity versus incidence angle is generated. The presence of an analyte on the surface of the test element will change the angle at which the minimum reflection is obtained due to surface plasmon resonance coupling.

Returning to Figure 1, the analysis described below is typically performed by a processor 124, with or without a storage medium, that is coupled to the detection device 116 to receive the signal. This analysis is performed by software, hardware, or a combination thereof. According to another embodiment, this same analysis is

accomplished using discrete or semi-programmable hardware configured, for example, using a hardware descriptive language, such as Verilog. In yet another embodiment, the analysis is performed using a processor having at least one look-up table arrangement with data stored therein to represent the complete result or partial results of the equations below based on a given set of input data, the input data corresponding to parameters used on the right side of the equations.

Position Determination of a Deviation from a Baseline

The following methods can be used to determine a position of a deviation from a baseline in a signal such as, for example, a surface plasmon resonance spectrum. It will be recognized that these methods can be used with signals other than surface plasmon resonance spectra. Moreover, it will be recognized that an unrefined signal from a detection device, such as detection device 116 of Figure 1, may be further refined before it is analyzed using the methods described herein. Examples of refinements are discussed in a subsequent section.

Figure 4 illustrates a signal 200 having a deviation 202 from a baseline 204 of the signal. The deviation can be, for example, a "notch" in the signal, as illustrated in Figure 4; the "notch" extending downward from the baseline. A "notch" can also be referred to as a "valley". In other embodiments, the deviation is a "peak" which extends upward from the baseline. The methods and devices described herein can be used with both notches and peaks. The deviation (e.g., notch or peak) from the baseline can indicate the presence of an analyte or may be modified by the presence of the analyte. The relative position of the deviation 202 can, at least in some instances, provide useful information, as described above for surface plasmon resonance.

A method, according to the invention, for determining the relative position of the deviation 202 includes transforming the signal using a Fourier transform technique to obtain at least one pair of Fourier coefficients. These coefficients can then be used to determine the relative position of the deviation 202.

For signals, such as that illustrated in Figure 4, with N discrete points, k = 0, 1, 2, ..., N-1, and associated signal magnitudes, x_k, the Fourier transform has the form:

$$y_p = \sum_{k=0}^{N-1} x_k (\cos(2\pi kp / N) + i\sin(2\pi kp / N)) = y_{p,r} + iy_{p,i} \qquad 1)$$

where p = 0, 1, 2, ..., N-1, $y_{p,r}$ is the real portion of y_p, and $y_{p,i}$ is the imaginary portion of y_p. Reference to "a pair of Fourier coefficients" is directed to the pair $y_{p,i}$ and $y_{p,r}$ for a single value of p. For the case where all x_k are real, the real and imaginary portions of y_p become:

$$y_{p,r} = \sum_{k=0}^{N-1} x_k \cos(2\pi kp / N) \qquad 2)$$

$$y_{p,i} = \sum_{k=0}^{N-1} x_k \sin(2\pi kp / N) \qquad 3)$$

In this instance, $y_{p,r}$ can be referred to as a "Fourier cosine coefficient" and $y_{p,i}$ can be referred to as a "Fourier sine coefficient".

For any y_p where $p>0$, a phase angle can be determined between the real and imaginary portions from the following equation:

$$\phi_p = \arctan(y_{p,i} / y_{p,r}) \qquad 4)$$

The phase angle can be correlated to the relative position of the deviation in the signal.

Although the phase angle itself can be correlated to relative position, in some instances, the phase angle is multiplied by a scaling factor to give the relative position of the deviation. One example of a suitable scaling factor includes multiplying the calculated phase angle by $N/2\pi$.

Figure 5 illustrates a series of 31 signals where the deviation is moved to the left for each subsequent signal. Figure 6 is a graph the first harmonic phase angle, ϕ_1, multiplied by a scaling factor, for each of the 31 signals. As illustrated in Figure 6, the phase angle has a linear relationship to the position of the deviation, thereby allowing one to determine relative position of a deviation or a change in position of a deviation by determination of the phase angle. Although the first harmonic phase angle was used in the illustration, it will be recognized that other harmonic phase angles (e.g, the second harmonic phase angle, the third harmonic phase angle, etc.) can be used, if desired.

Any Fourier transform technique can be used, including, for example, Fast Fourier Transform (FFT) techniques, such as, for example, the Cooley-Tukey FFT algorithm. It will be recognized that, although a phase angle can be determined by Fourier transform of the signal, the phase angle can also be calculated by determining only the desired coefficients, $y_{p,r}$ and $y_{p,i}$, using, for example, equations 2) and 3).

Application Example - Surface Plasmon Resonance Signals

Figure 7 illustrates a surface plasmon resonance signal. Typically, the signal is not ready for analysis using the Fourier coefficients without further refinement. A variety of methods are used to refine the signal. These methods can be used in the order presented below or they can be used in different orders. In addition,

refinement of the signal can include all or only some of the methods described below.

The signal from the detection device can be refined by combining the signal with a background signal to reduce or eliminate effects such as, for example, wavelength dependence of the intensity of light from the light source, absorption of light by the elements in the device 100 (e.g., the reflective metal layer, the test material, analyte, etc.), and the wavelength dependence of the detection device. Figure 8 illustrates a background signal (from a region of the surface without a grating) associated with the signal of Figure 7.

In one embodiment of the device, each point in the signal is divided by the corresponding point in the background signal. Figure 9 is a convoluted signal formed by dividing each point in the signal of Figure 7 by the corresponding point in the background signal of Figure 8. In another embodiment, the background signal is subtracted, point-by-point, from the signal.

Another refinement addresses possible odd-even bias for the points of the signal arising from the detection device or another portion of the device 100. One embodiment of this refinement includes, for each particular point, adding the values of the neighboring points to twice the value of the particular point (e.g., $x_k' = (x_{k-1} + 2x_k + x_{k+1})/4$). For the first and last data points, which have only one neighbor, the original points can be used or an average of the point and its neighbor can be calculated. Typically, these points are significantly far away from the deviation to make little difference. Figure 10 illustrates the signal from Figure 9 after this refinement has been applied.

The data can be smoothed by taking, for each particular point, an average of the range of points extending before and after the particular point. For example, for x_k, a range of m points will typically extend from $x_{k-(m-1)/2}$ to $x_{k+(m-1)/2}$. For example, a smoothing window of 15 points would result in the following calculation for each x_k for k=0 to N-1:

$$x_k' = \frac{1}{15}\sum_{m=k-7}^{k+7} x_m$$

Typically, points at the beginning and end of the signal will use the values for the first or last point, respectively, to fill out the range for m<0 or m>N-1. Figure 11 illustrates the signal from Figure 10 after applying a smoothing window of 15 points.

Another optional refinement includes normalizing the range of the x_k values. For example, the minimum value can be subtracted from each of the x_k values so that the refined values range from zero. In addition or alternatively, the x_k values can be multiplied by a factor corresponding to: Range/(max(x_k) - min(x_k)) where Range is

the desired range of values, $\max(x_k)$ is the maximum value of x_k for all k, and $\min(x_k)$ is the minimum value of x_k for all k. The combination of these two refinements stretches the signal from a value of zero to a value corresponding to Range. Figure 12 illustrates the signal from Figure 11 after applying these two refinements.

Another refinement includes clipping the signal to provide a smooth baseline. In this refinement, all x_k>Clip Value are made equal to the Clip Value. The Clip Value is chosen to be less than any deviation from the baseline due to noise, but significantly greater than the minimum value of the notch. This generates a straight baseline with only the deviation varying from the baseline, as illustrated in Figure 13.

Additional refinements can be made to assist in the Fourier transformation and determination of the phase angle. Typically, Fast Fourier Transformation techniques require that the number of points be an even integral power of two. Accordingly, the signal can be expanded to that number of points by adding points where the x_k value is equal to the baseline value from the signal (e.g., Clip Value if the clipping refinement is used).

In addition, the number of points can be similarly expanded to address ambiguities arising because the phase angle is determined using an arctangent relationship. The arctangent function is undefined at odd multiples of $\pi/2$. Accordingly, the number of points in the signal that is transformed should be chosen so that the calculated phase angle is between 0 and $\pi/2$. The first harmonic frequency (corresponding to p=1 in equations 1-3 above) has a period equal to the number of points that are in the signal to be Fourier transformed. To ensure that the phase angle is in the first quadrant (i.e., between 0 and $\pi/2$), the deviation from the baseline should be within the first quarter of points in the signal. Accordingly, the signal can be expanded by adding points at the end of the signal, using an x_k value equal to the baseline, to provide at least 4N points, where N is the number of points in the original signal from the detection device. Thus, the original signal is expanded by the addition of at least three times the number of original points. For phase angles calculated for other harmonic frequencies (e.g., the second or third harmonic frequencies), the number of points must be increased to ensure that the phase angle ranges from 0 to $\pi/2$.

Once the desired refinements are performed, the signal is prepared for calculation of the Fourier coefficients described above. If the signal contains two or more deviations that are separated from each other, the signal can be divided into individual windows, each containing one deviation, and individually processed.

The above-described method for position determination of a deviation from a baseline is useful in the analysis of other optical spectra and other signals where the position of a deviation from a baseline yields information regarding a condition of the system being interrogated. Other areas in which this technique can be useful include, for example, other spectroscopic methods and communications decoding.

The present invention should not be considered limited to the particular examples described above, but rather should be understood to cover all aspects of the invention as fairly set out in the attached claims. Various modifications, equivalent processes, as well as numerous structures to which the present invention may be applicable will be readily apparent to those of skill in the art to which the present invention is directed upon review of the instant specification.

WHAT IS CLAIMED IS:

1. A method of detecting a position of a deviation from a baseline of a signal, the method comprising steps of:

generating at least one pair of Fourier coefficients from the signal;

determining a phase angle from a one of the at least one pair of Fourier coefficients; and

correlating the phase angle to the position of the deviation from the baseline of the signal.

2. The method of claim 1, wherein the step of generating at least one pair of Fourier coefficients comprises generating at least one pair of Fourier coefficients by Fourier transforming the signal.

3. The method of claim 2, wherein generating at least one pair of Fourier coefficients comprises generating at least one pair of Fourier coefficients by Fast Fourier Transformation of the signal.

4. The method of claim 1, wherein the step of generating at least one pair of Fourier coefficients comprising generating at least one pair of Fourier coefficients, each of the at least one pair of Fourier coefficients comprising a Fourier sine coefficient and a Fourier cosine coefficient.

5. The method of claim 4, wherein the step of generating at least one pair of Fourier coefficients comprises generating a pair of Fourier coefficients, $y_{p,r}$ and $y_{p,i}$, wherein

$$y_{p,r} = \sum_{k=0}^{N-1} x_k \cos(2\pi kp / N) \qquad 2)$$

$$y_{p,i} = \sum_{k=0}^{N-1} x_k \sin(2\pi kp / N) \qquad 3)$$

wherein the signal contains N discrete points, k = 0, 1, 2, ..., N-1, with associated signal magnitudes, x_k, and p is an integer selected from the group of integers ranging from 1 to N-1.

6. The method of claim 5, wherein the step of determining a phase angle comprises determining a phase angle, ϕ_p, wherein $\phi_p = \arctan(y_{p,i}/y_{p,r})$.

7. The method of claim 6, wherein the step of determining a phase angle comprises determining a phase angle, ϕ_p, wherein $\phi_p = \arctan(y_{p,i}/y_{p,r})$ and p=1.

8. The method of claim 1, further comprising steps of:
obtaining an unrefined signal from a detection device; and
refining the unrefined signal to generate the signal and produce the baseline.

9. The method of claim 8, wherein refining the unrefined signal comprises extending the signal by at least three times the number of points in the unrefined signal.

10. The method of claim 8, wherein refining the unrefined signal comprises obtaining the signal from a combination of the unrefined signal and a background signal.

11. The method of claim 1, further comprising steps of:
generating the signal using a detection device, wherein the signal is an optical spectrum.

12. The method of claim 11, further comprising steps of:
generating the signal using a detection device, wherein the signal is a surface plasmon resonance spectrum.

13. The method of claim 11, wherein the step of generating the signal comprises
irradiating a surface with light; and
generating the signal by measuring, for individual wavelengths in a range of wavelengths, an intensity of reflected light using the detection device.

14. The method of claim 13, wherein the surface comprises a diffraction grating.

15. The method of claim 14, further comprising disposing a sample over the diffraction grating.

16. An apparatus, comprising:
a detection device; and
a processor coupled to the detection device and configured and arranged to detect a position of a deviation from a baseline of a signal generated by the detection device by:
generating at least one pair of Fourier coefficients from the signal;

determining a phase angle from a one of the at least one pair of Fourier coefficients; and

correlating the phase angle to the position of a deviation from a baseline of the signal.

17. The apparatus of claim 16, further comprising a light source and a test element, the test element comprising a reflective metal layer, the light source illuminating the reflective metal layer and the detection device generating the signal in response to light reflected from the reflective metal layer.

18. The apparatus of claim 16, wherein the processor is configured and arranged to generate a pair of Fourier coefficients, $y_{p,r}$ and $y_{p,i}$, wherein

$$y_{p,r} = \sum_{k=0}^{N-1} x_k \cos(2\pi kp / N) \qquad 2)$$

$$y_{p,i} = \sum_{k=0}^{N-1} x_k \sin(2\pi kp / N) \qquad 3)$$

wherein the signal contains N discrete points, k = 0, 1, 2, ..., N-1, with associated signal magnitudes, x_k, and p is an integer selected from the group of integers ranging from 1 to N-1.

19. The apparatus of claim 18, wherein the processor is configured and arranged to determine a phase angle, ϕ_p, wherein $\phi_p = \arctan(y_{p,i}/y_{p,r})$.

20. The apparatus of claim 16, wherein the processor is configured and arranged to refine a signal from the detection device prior to generating the at least one pair of Fourier coefficients from the signal.

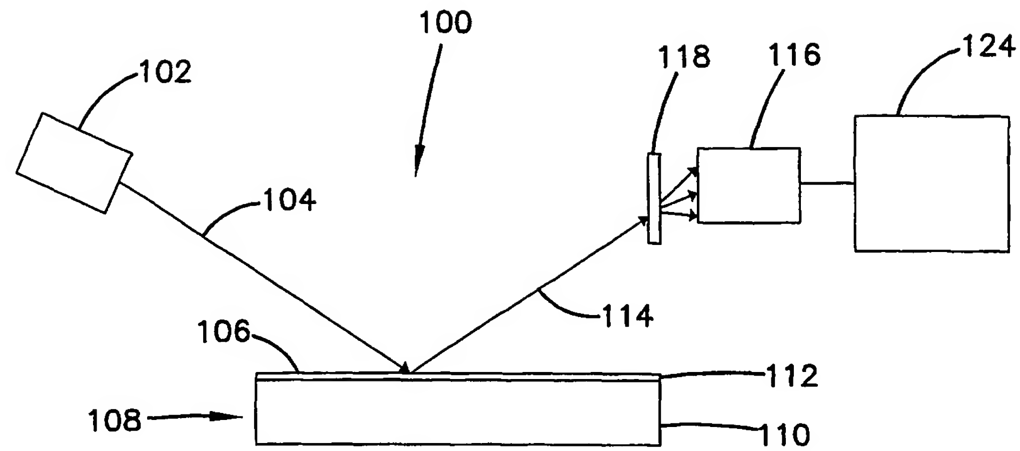

100
102
104
106
108
110
112
114
116
118
124

FIG. 1

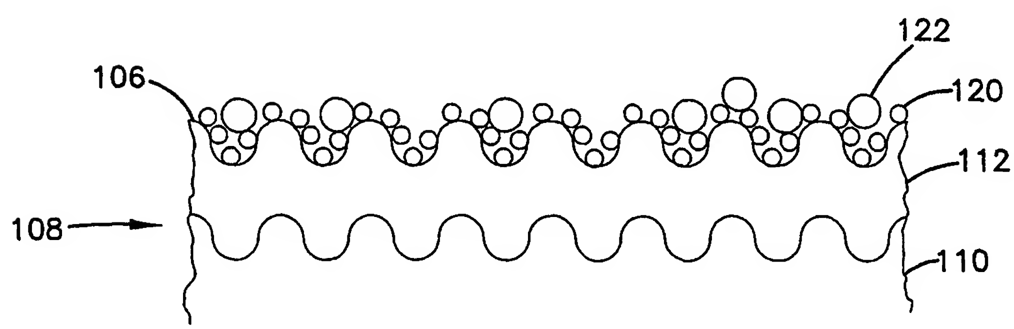

106
108
110
112
120
122

FIG. 2

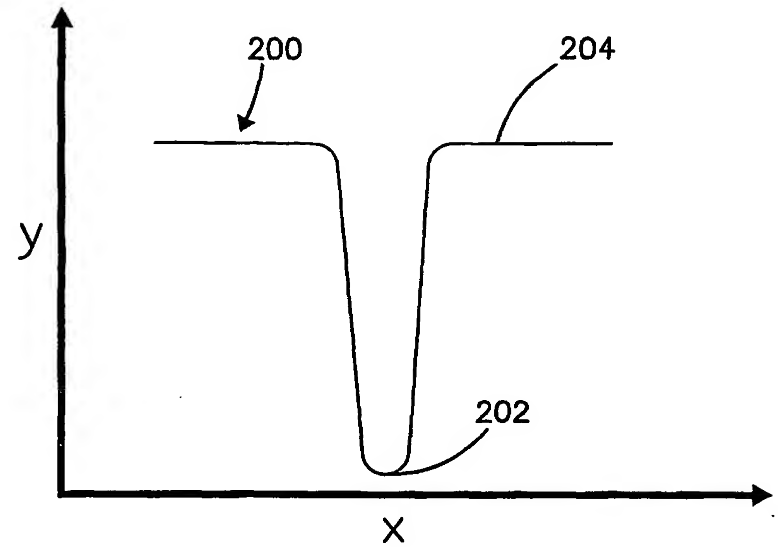


FIG. 4

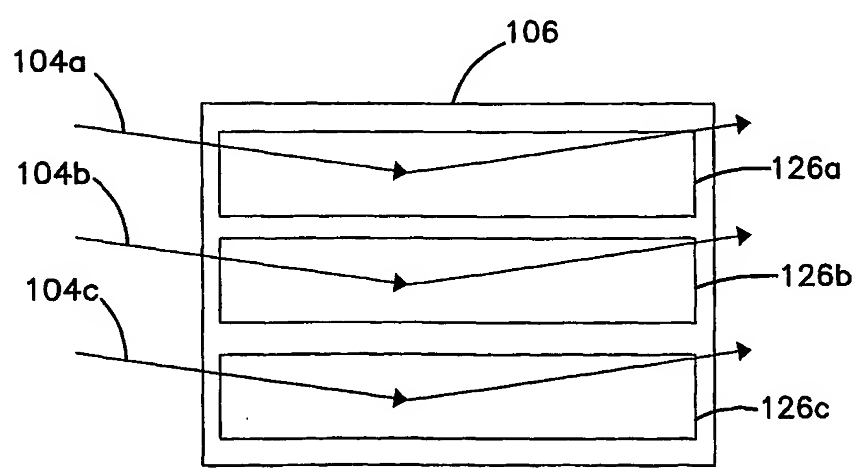


FIG. 3

FIG. 5

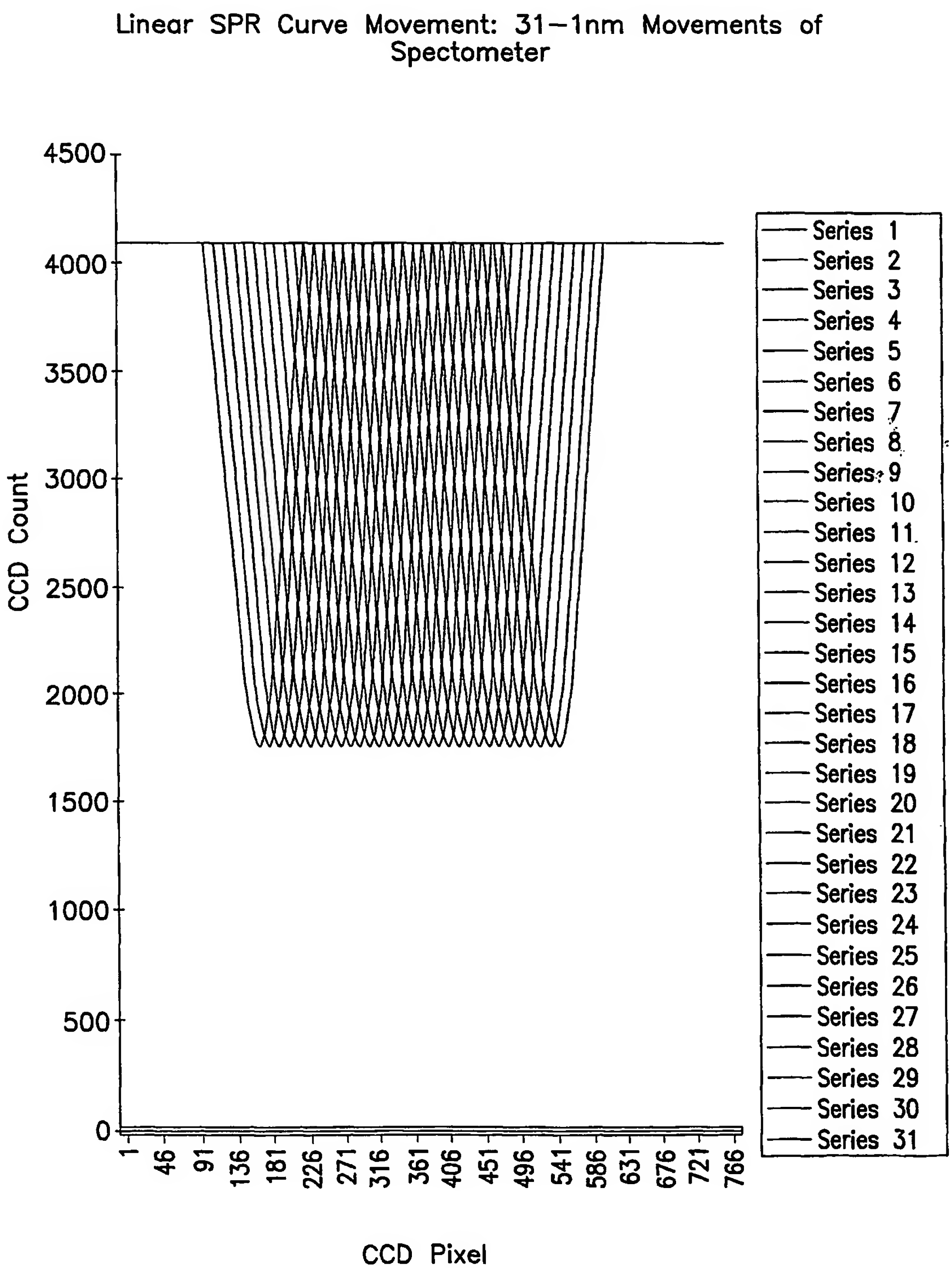

Linear SPR Curve Movement: 31-1nm Movements of Spectometer
4500
4000
3500
3000
2500
2000
1500
1000
500
0
CCD Count
1
46
91
136
181
226
271
316
361
406
451
496
541
586
631
676
721
766
CCD Pixel
Series 1
Series 2
Series 3
Series 4
Series 5
Series 6
Series 7
Series 8
Series 9
Series 10
Series 11
Series 12
Series 13
Series 14
Series 15
Series 16
Series 17
Series 18
Series 19
Series 20
Series 21
Series 22
Series 23
Series 24
Series 25
Series 26
Series 27
Series 28
Series 29
Series 30
Series 31

FIG. 6

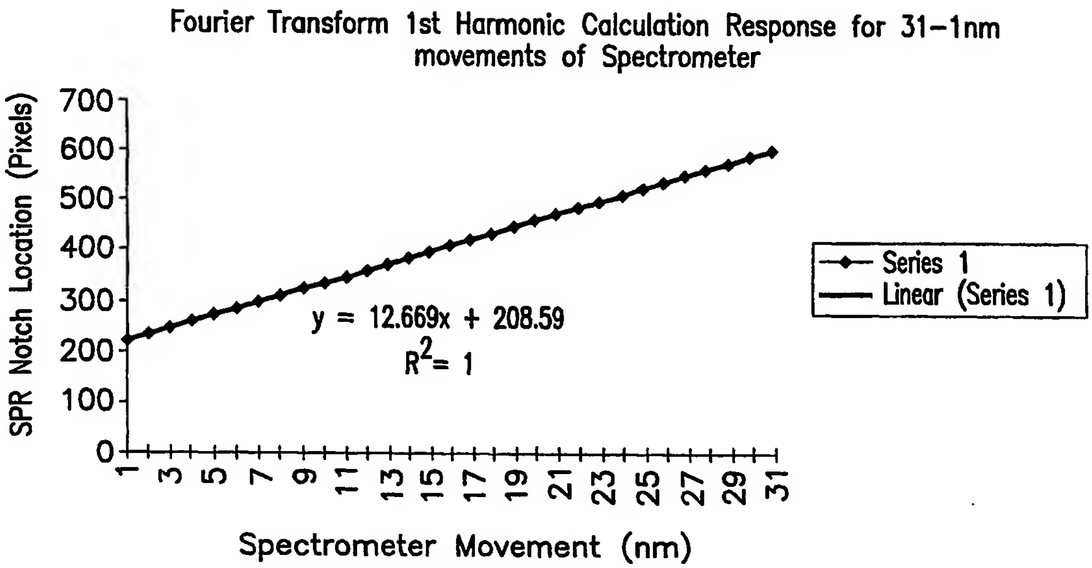

Fourier Transform 1st Harmonic Calculation Response for 31-1nm movements of Spectrometer
SPR Notch Location (Pixels)
700
600
500
400
300
200
100
0
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
31
Spectrometer Movement (nm)
y = 12.669x + 208.59
R2= 1
Series 1
Linear (Series 1)

FIG. 7

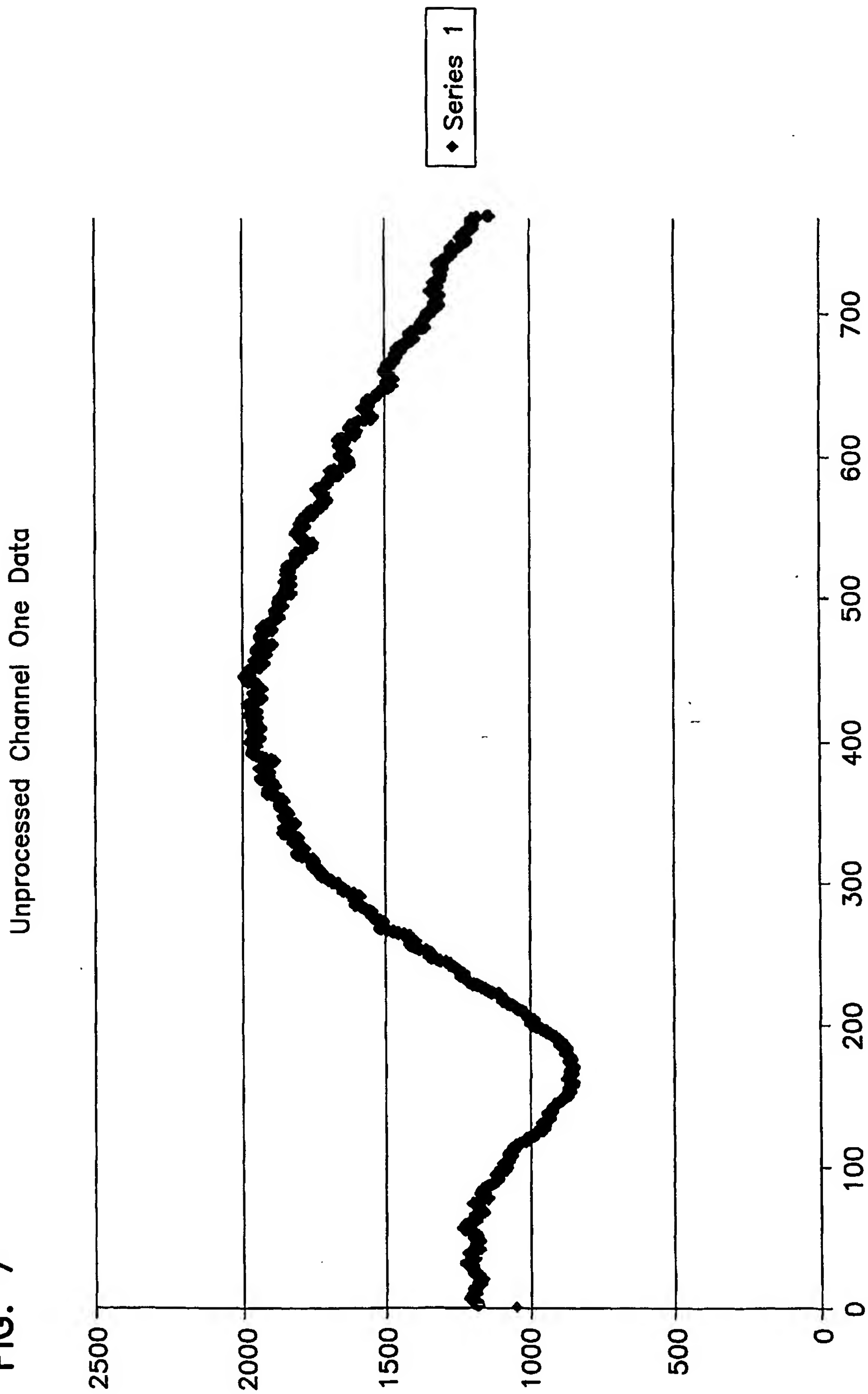

Unprocessed Channel One Data
Series 1
2500
2000
1500
1000
500
0
0
100
200
300
400
500
600
700

FIG. 8

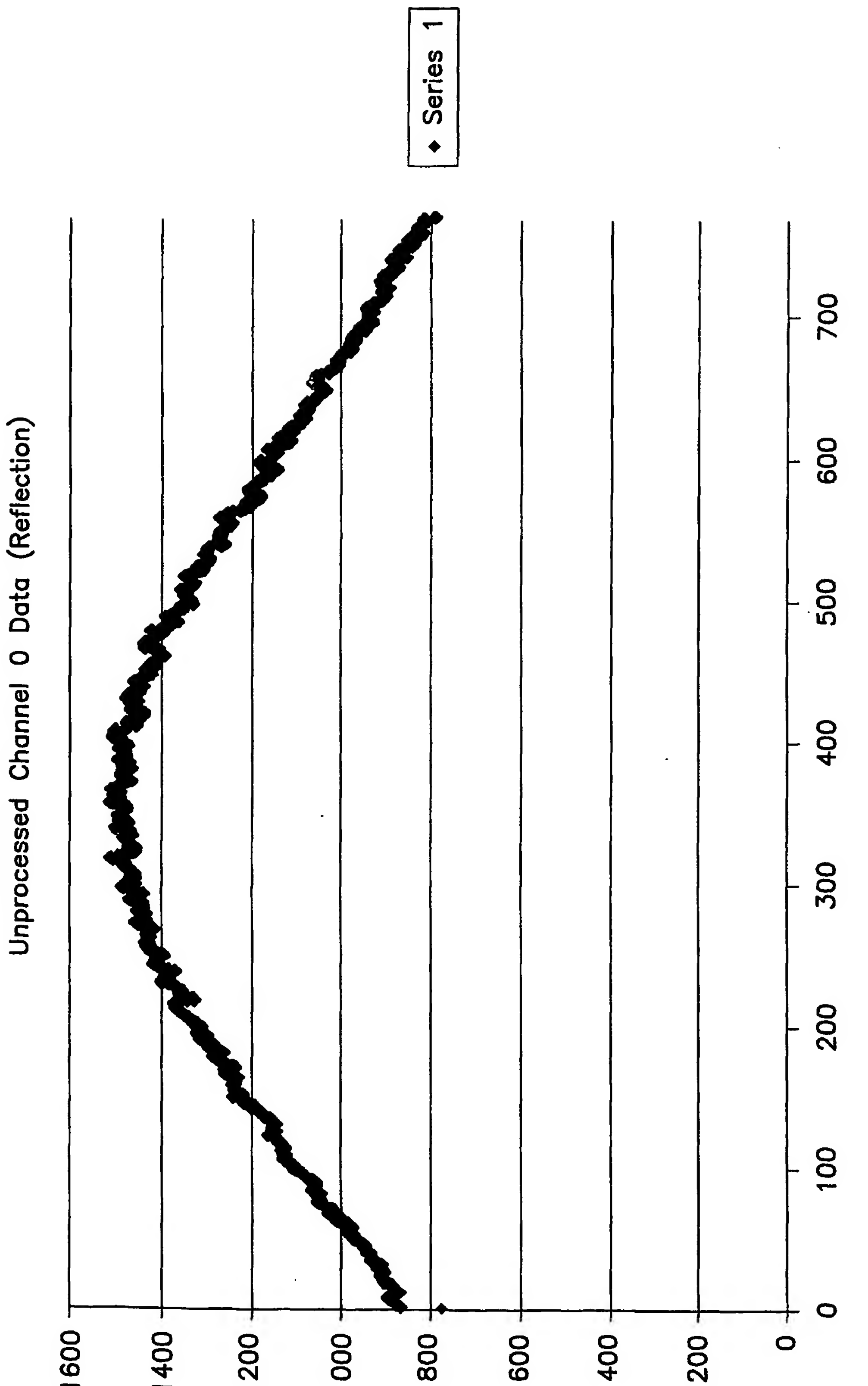

Unprocessed Channel 0 Data (Reflection)
Series 1
1600
1400
1200
1000
800
600
400
200
0
0
100
200
300
400
500
600
700

FIG. 9

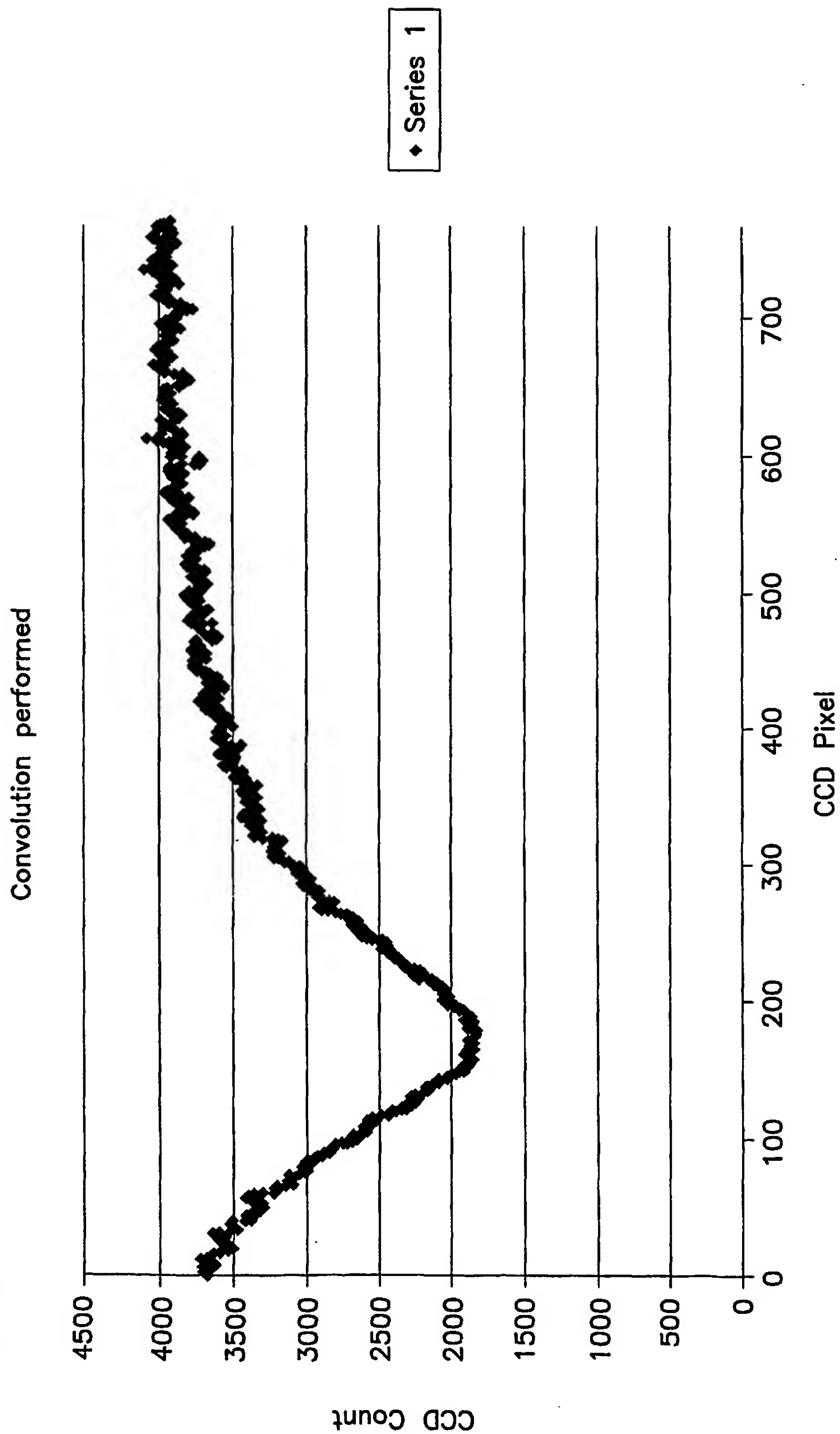

Convolution performed
Series 1
CCD Count
4500
4000
3500
3000
2500
2000
1500
1000
500
0
CCD Pixel
0
100
200
300
400
500
600
700

FIG. 10

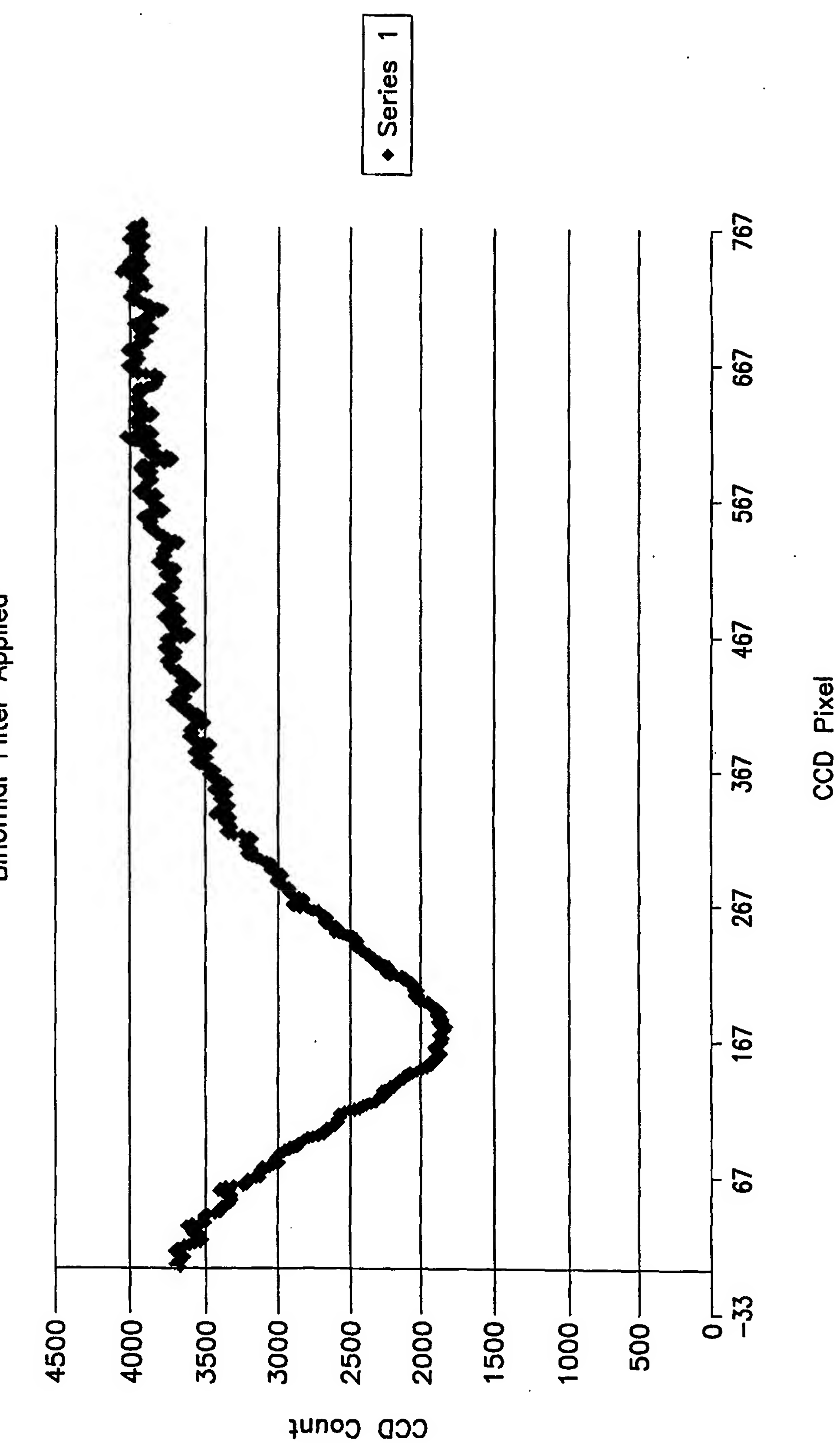

Binomial Filter Applied
Series 1
CCD Count
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-33
67
167
267
367
467
567
667
767
CCD Pixel

FIG. 11

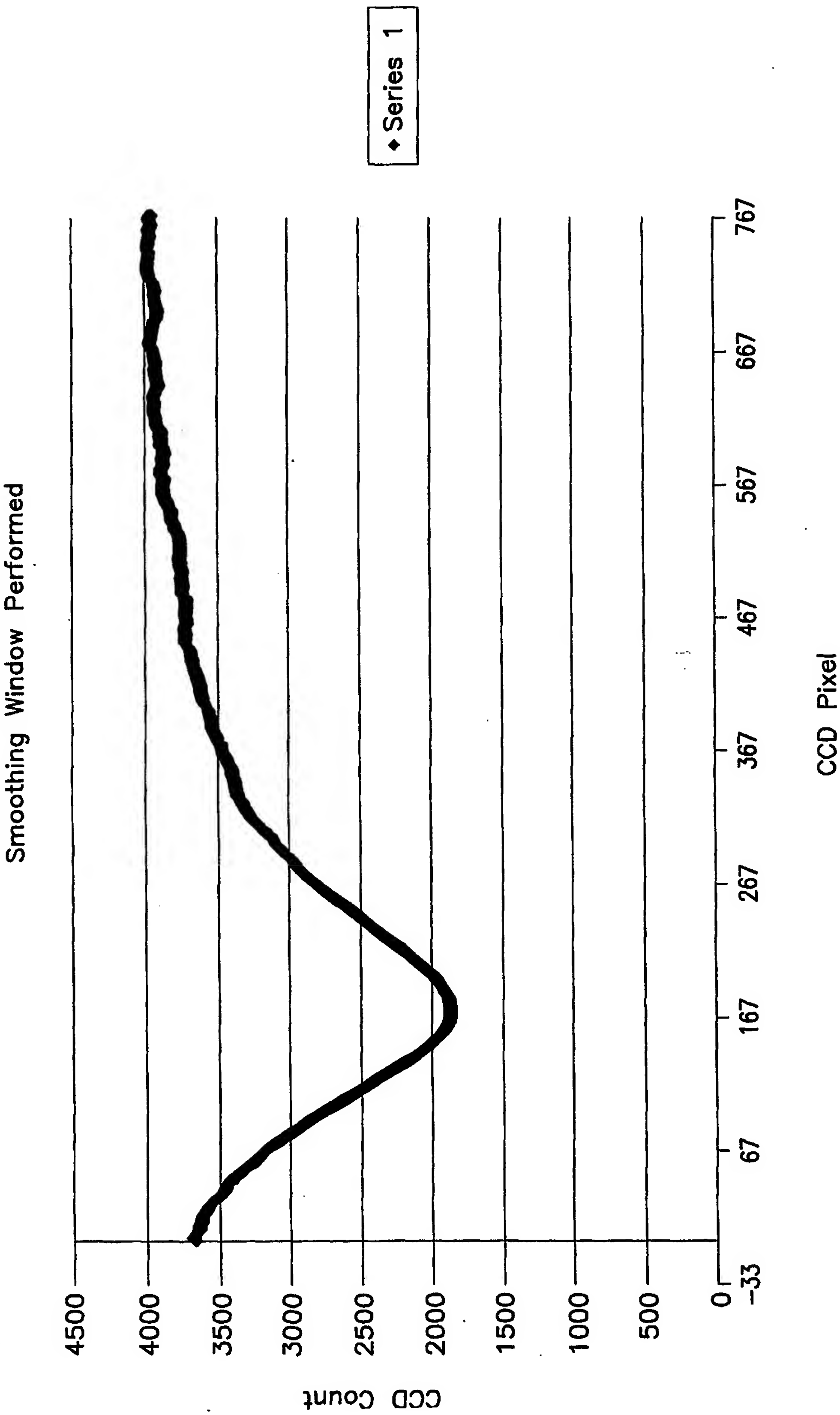

Smoothing Window Performed
Series 1
CCD Count
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-33
67
167
267
367
467
567
667
767
CCD Pixel

FIG. 12

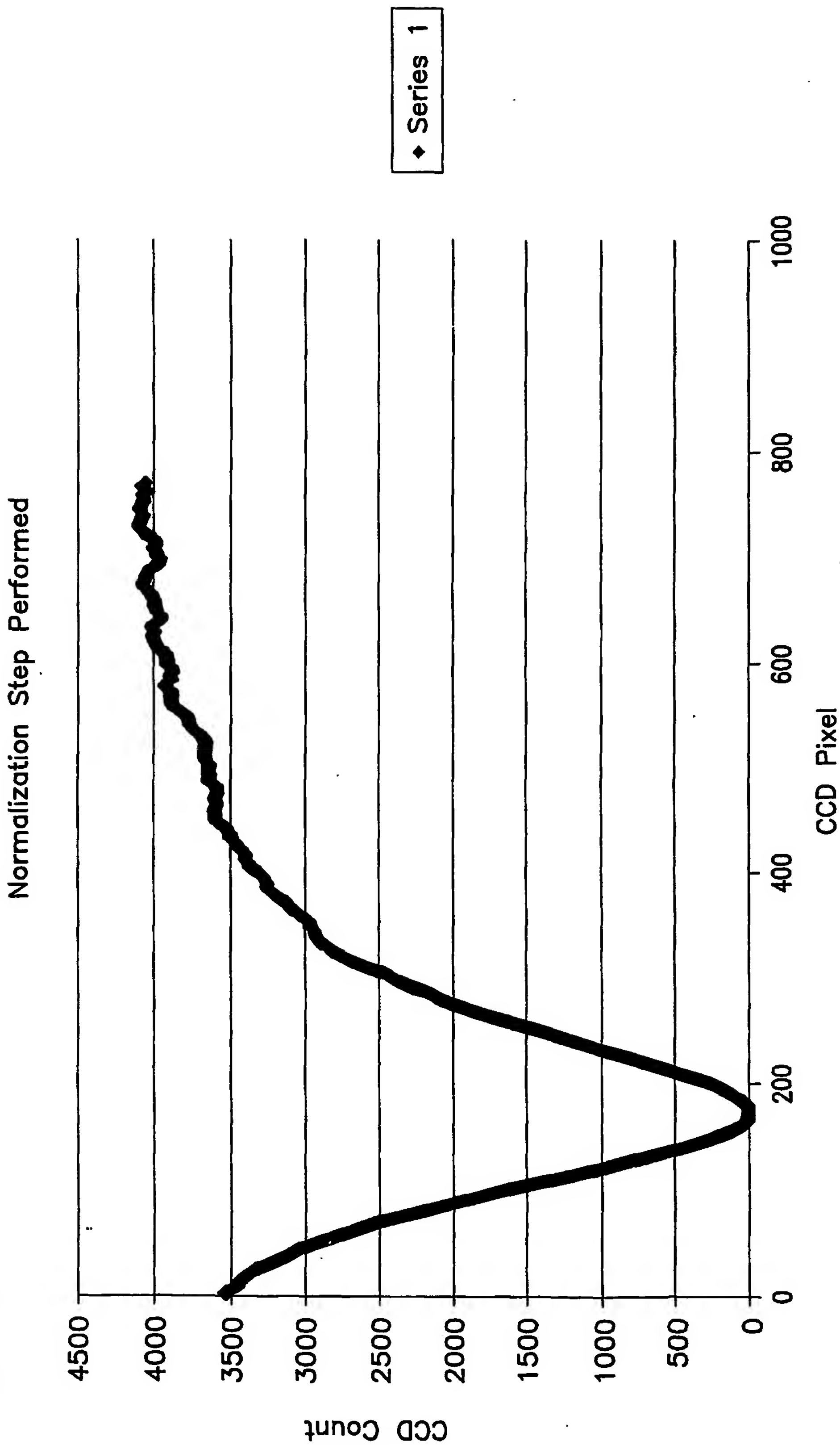
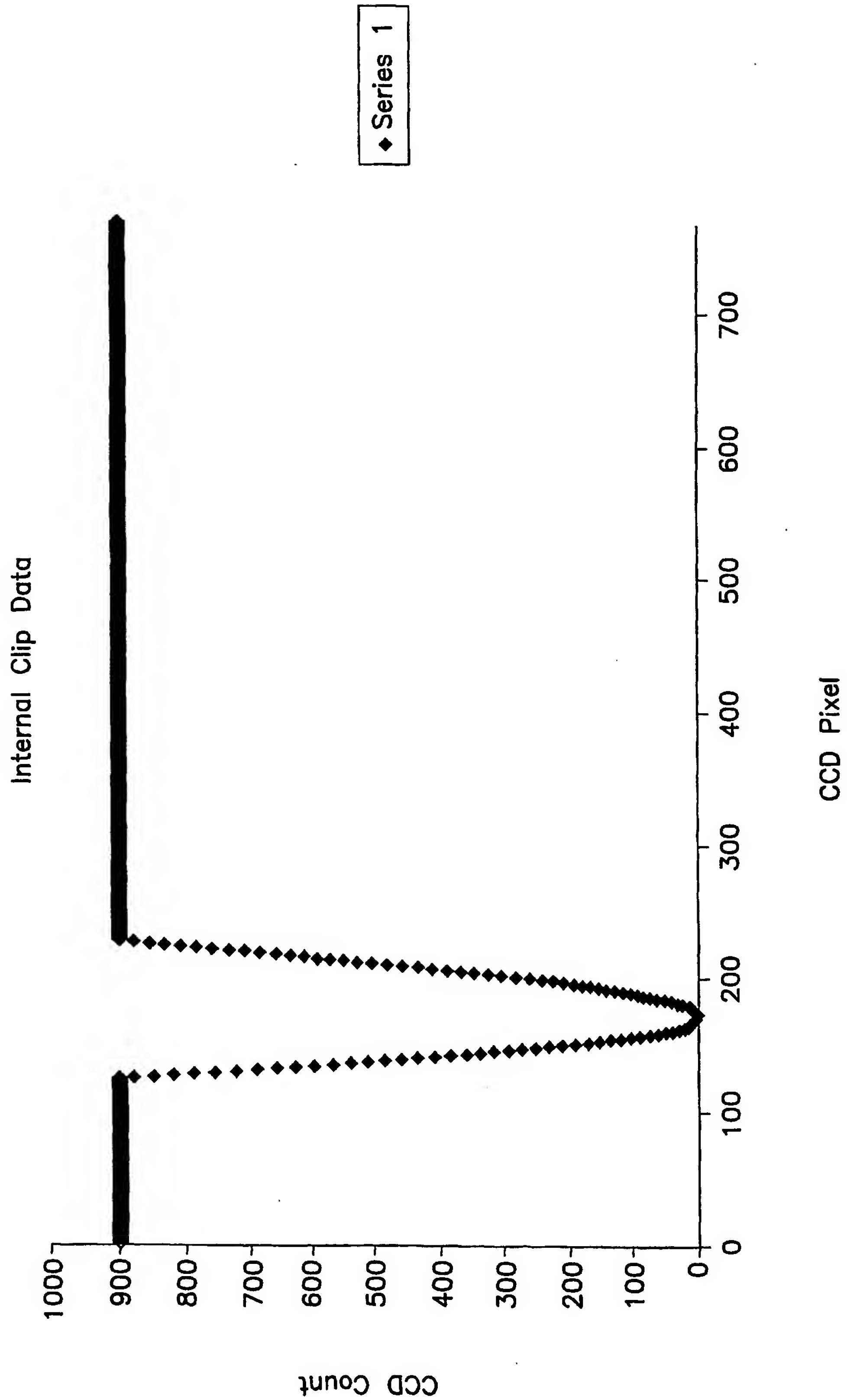

Normalization Step Performed
Series 1
4500
4000
3500
3000
2500
2000
1500
1000
500
0
CCD Count
0
200
400
600
800
1000
CCD Pixel

FIG. 13


Internal Clip Data
Series 1
CCD Count
CCD Pixel
1000
900
800
700
600
500
400
300
200
100
0
0
100
200
300
400
500
600
700

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 November 2001 (08.11.2001)

PCT

(10) International Publication Number
WO 01/84120 A3

(51) International Patent Classification⁷: G06F 17/10

(21) International Application Number: PCT/US01/14292

(22) International Filing Date: 2 May 2001 (02.05.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/564,140 3 May 2000 (03.05.2000) US

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(74) Agent: BRUESS, Steven, C.; Merchant & Gould P.C., P.O. Box 2903, Minneapolis, MN 55402-0903 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

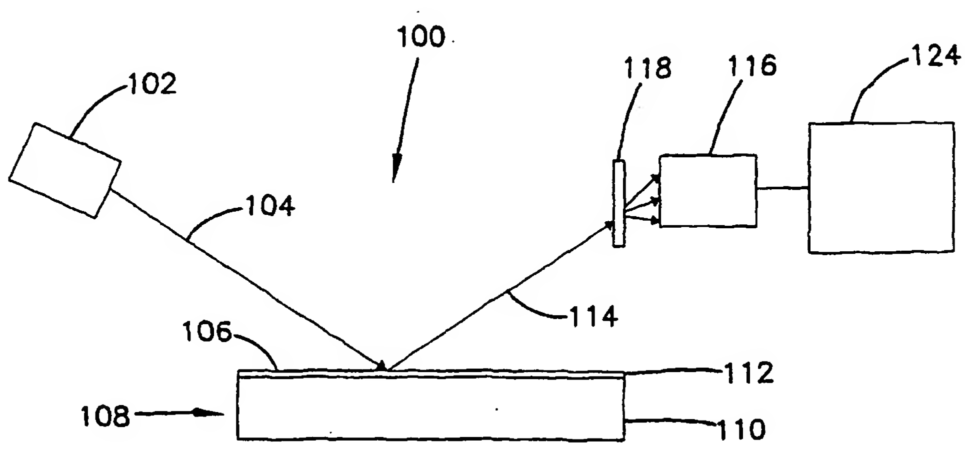
Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

Published:
— *with international search report*

(88) Date of publication of the international search report: 23 May 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS AND DEVICES FOR SIGNAL POSITION ANALYSIS



(57) Abstract: A method of detecting a deviation from a baseline of a signal includes generating at least one pair of Fourier coefficients from the signal. A phase angle is then determined from a pair of the Fourier coefficients and the phase angle is correlated to the position of the deviation from the baseline of the signal. Another embodiment is an apparatus that includes a processor that is configured and arranged to carry out the steps in the method. The method and apparatus can be used to analyze a variety of signals including optical spectra and telecommunications signals. One particular exemplified example is the analysis of surface plasmon resonance signals.

WO 01/84120 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/14292

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G06F17/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G06F G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

INSPEC, EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHU-XIONG DING ET AL: "Peak position estimation algorithms for cross-correlation function in elastography" PROCEEDINGS OF THE 20TH ANNUAL INTERNATIONAL CONFERENCE OF THE IEEE ENGINEERING IN MEDICINE AND BIOLOGY SOCIETY. VOL.20 BIOMEDICAL ENGINEERING TOWARDS THE YEAR 2000 AND BEYOND (CAT. NO.98CH36286), PROCEEDINGS OF THE 20TH ANNUAL INTERNATIONAL CONFEREN, pages 866-868 vol.2, XP002187549 1998, Piscataway, NJ, USA, IEEE, USA ISBN: 0-7803-5164-9 --- -/--	

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17 January 2002	30/01/2002

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A	MORANDI C ET AL: "Digital image registration by phase correlation between boundary maps" IEE PROCEEDINGS E (COMPUTERS AND DIGITAL TECHNIQUES), MARCH 1987, UK, vol. 134, no. 2, pages 101-104, XP001058273 ISSN: 0143-7062	
A	GB 2 247 749 A (MARCONI GEC LTD) 11 March 1992 (1992-03-11)	

INTERNATIONAL SEARCH REPORT

.ıformation on patent family members

Inte· 'ional Application No
PC ı/US 01/14292

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 2247749	A	11-03-1992	NONE	

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